Methodological Challenges for Secondary Prevention Trials in PTSD

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Goal of Secondary Prevention

- To prevent the development of PTSD and other consequences of traumatic stress exposure
- May involve a prophylactic intervention in high risk individuals (e.g. “Battlemind” training)
- May involve a blanket approach to everyone exposed to a traumatic event (“Re-Set” training-DoD)
- May involve an intervention to a targeted subgroup at high risk for PTSD

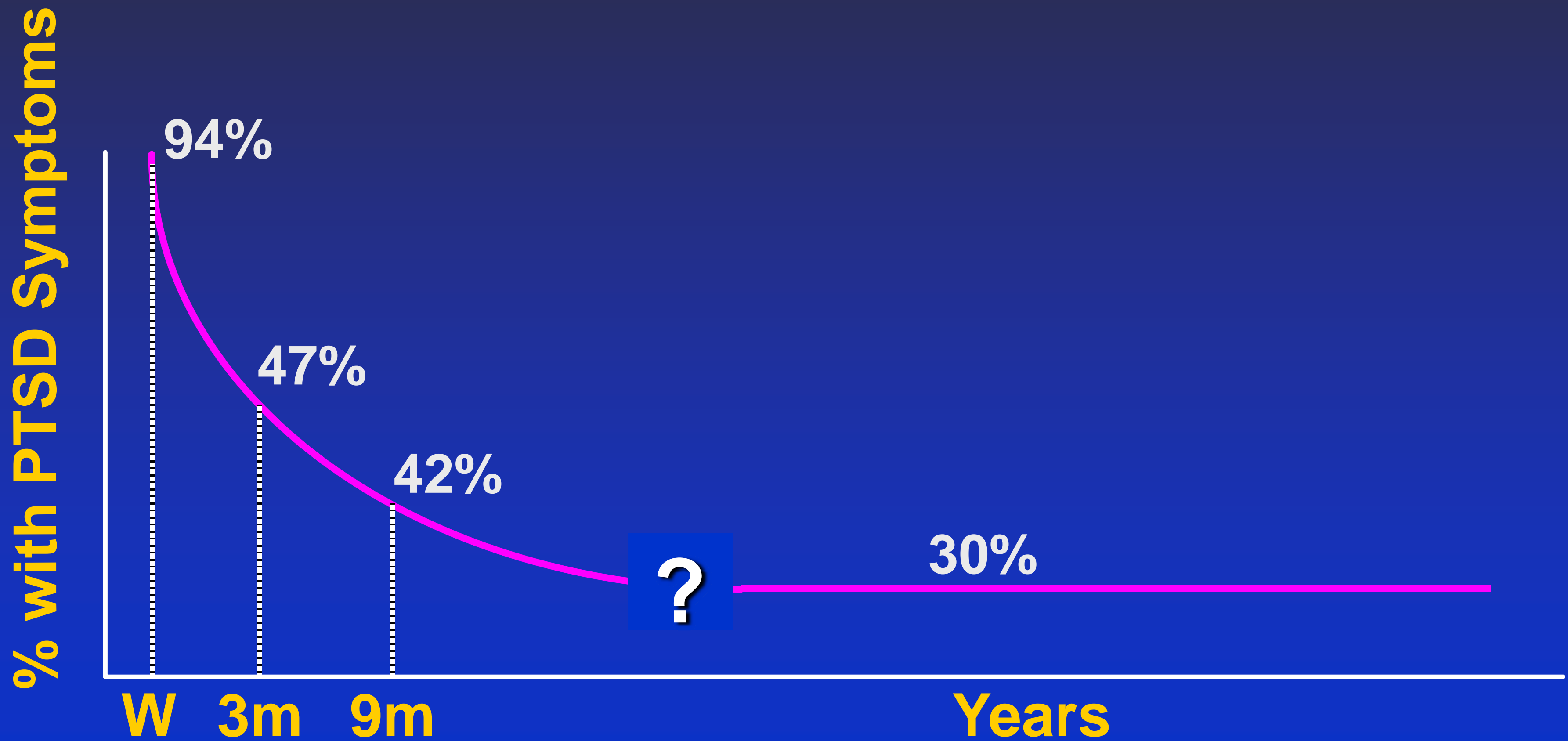
Early Intervention for Trauma: Where Are We and Where Do We Need to Go? A Commentary

- Brett T. Litz, Ph.D.
- Journal of Traumatic Stress, Vol. 21, No. 6, December 2008, pp. 503–506

Problems with Nontargeted Intervention

- When to intervene?
  - Immediate (0-48 hours) versus acute (0-4 weeks)
- Lessons learned from Debriefing
- Psychological First Aid
- May be intrusive and not feasible
- May need to focus on education and reducing stigma for seeking care

Longitudinal Course of PTSD Symptoms



Kessler RC, et al. Arch Gen Psychiatry. 1995;52:1048-60.

Identifying High Risk Subgroups

- Requires prospective studies of high risk individuals
- Most longitudinal studies involve subjects recruited post exposure
  - Has practical and economic advantages
  - Suffers from selection bias and retrospective biases
- Military and First Responders are good samples to start with despite problems with generalizability

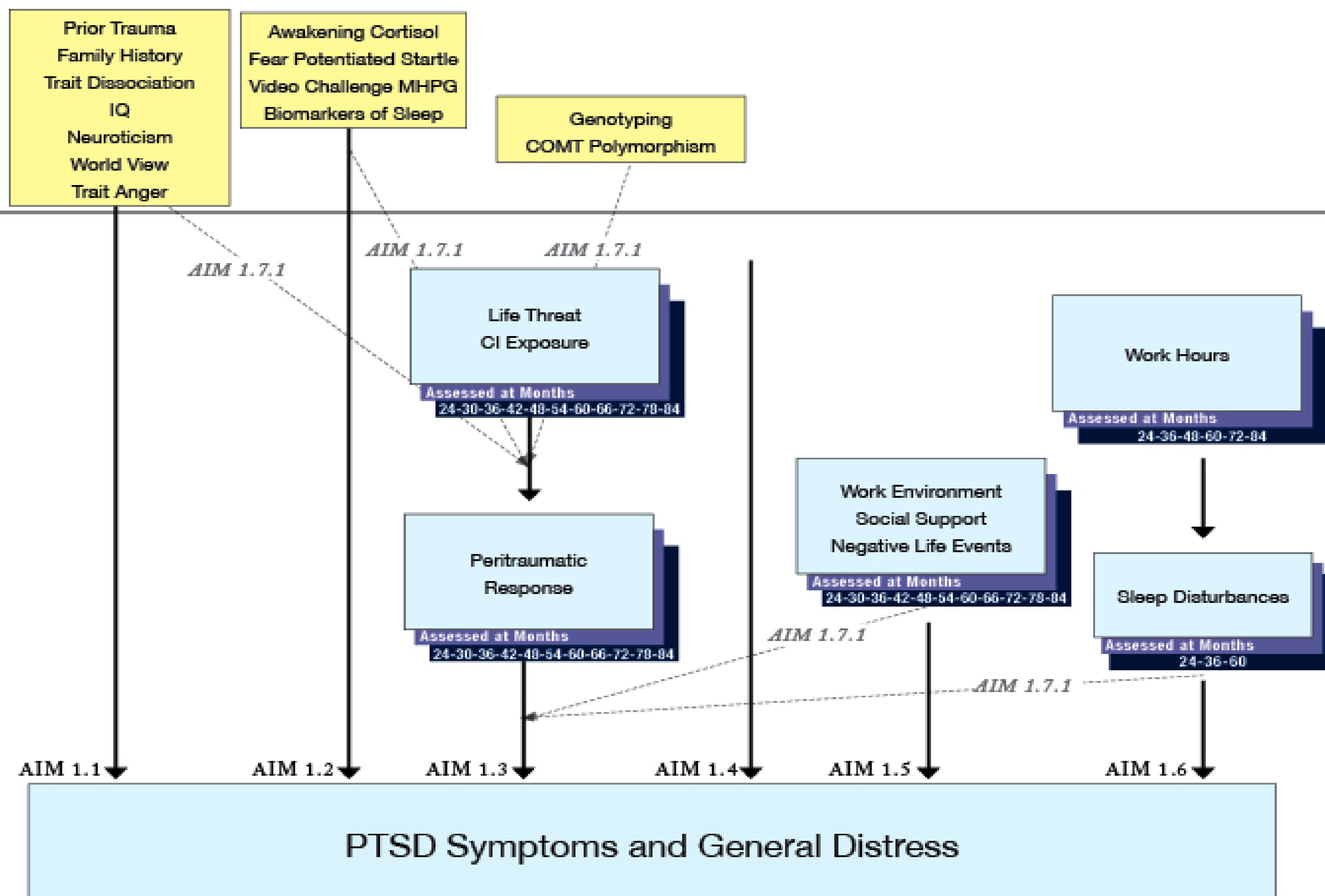
Risk Factors for PTSD

- Severity of trauma (ie, threat, duration, injury, loss)
- Prior traumatization
- Gender
- Ethnicity
- Prior mood and/or anxiety disorders
- Family history of mood or anxiety disorders
- Education

Using Peritraumatic Predictors of High Risk for PTSD

- Dissociation
  - Shalev, et al. Am J Psychiatry. 1996 ;153:219-225.; Marmar, et al. Am J Psychiatry. 1994;151:902-907, Marmar, et al. Am J Psychiatry. 1996;153(7 Suppl):94-102.
- Distress
  - Bernat, et al. Am J Psychiatry. 1996 ;153(7 Suppl):94-102.; Brunet, et al. Am J Psychiatry. 2001;158:1480-5.
- Panic
  - Bernat, et al. J Trauma Stress. 1998;11:645-64.; Falsetti & Resnick et al. J Trauma Stress. 1997 Oct;10(4):683-9.; Galea, et al. N Engl J Med. 2002;28;346:982-7.
- Increased HR
  - Shalev, et al. Arch Gen Psychiatry. 1998;55:553-9.; McFarlane, et al. Ann N Y Acad Sci. 1997;821:437-41.; Zatzick, et al. Biol Psychiatry. 2005;57:91-5. HR> 95
- Low cortisol
  - Resnick, et al. Am J Psychiatry. 1995;152:1675-7.; McFarlane, et al. Ann N Y Acad Sci. 1997 Jun 21;821:437-41.
- Reduced Hippocampal Volume
  - Gilbertson/Pitman Nat Neurosci. 2002;5:1242-7.
- Low neuropeptide Y ?
  - Morgan, et al. Biol Psychiatry. 2000;40:902-9.

Prospective Study of Posttraumatic Stress Disorder in Police Officers



ACADEMY
BASELINE
POLICE
SERVICE
ASSESSMENTS
24 MONTHS
30 MONTHS
36 MONTHS
42 MONTHS
48 MONTHS
54 MONTHS
60 MONTHS
66 MONTHS
72 MONTHS
78 MONTHS
84 MONTHS
Individual Factors
Environmental Factors
Prior Trauma
Family History
Trait Dissociation
IQ
Neuroticism
World View
Trait Anger
Awakening Cortisol
Fear Potentiated Startle
Video Challenge MHPG
Biomarkers of Sleep
Genotyping
COMT Polymorphism
AIM 1.7.1
AIM 1.7.1
AIM 1.7.1
Life Threat
CI Exposure
Assessed at Months
24-30-36-42-48-54-60-66-72-78-84
Work Hours
Assessed at Months
24-36-48-60-72-84
Work Environment
Social Support
Negative Life Events
Assessed at Months
24-30-36-42-48-54-60-66-72-78-84
Peritraumatic
Response
Assessed at Months
24-30-36-42-48-54-60-66-72-78-84
Sleep Disturbances
Assessed at Months
24-36-60
AIM 1.7.1
AIM 1.7.1
AIM 1.1
AIM 1.2
AIM 1.3
AIM 1.4
AIM 1.5
AIM 1.6
PTSD Symptoms and General Distress

Brief Review of Secondary Prevention Trials: Pubmed and ClinicalTrials.gov

- CBT for Acute PTSD
  - 4-5 sessions @ 90 minutes, involves exposure therapy
- Self Help Booklet not helpful
- Debriefing not well supported
- Propranolol for Acute Stress Disorder
- Propranolol to prevent PTSD
- SSRIs: sertraline, escitalopram

Problems Encountered by Secondary Treatment Trials

- Recruitment
  - Must be embedded in E.D. setting
  - Often must subordinate to immediate critical care interventions
  - May have iatrogenic effects
- Retention
- Generalizability

Novel Approaches

- Must take long view of who will implement successful interventions
  - Likelihood of taking place in mental health treatment settings dependent on technical complexity of intervention
  - If mental health personnel are involved, ideally it would be in settings with integrated care
  - Likely will involve emergency care staff
  - May involve settings outside of traditional health care

Novel Approaches with Treatment Provided by Mental Health

- Telephone psychotherapy (e.g. CBT)
- Web interaction
- Cyber CBT

Novel Interventions Led by Non Mental Health Personnel

- Likely to involve Pharmacologic Agents, Psychoeducation, or Effective Referral Strategies
- May focus on non-stigmatized primary outcomes (e.g. sleep, pain, speed of physical recovery)
- Anesthesiologists (e.g. beta blocker studies)
- Critical Care and Burn Specialists (e.g. steroid use)
- Trauma Surgeons (Hypnotics, anti-adrenergic agents, etc.)
- Primary Care (Antidepressants, or any of the above)

Summary

- Access to effective treatment for the secondary prevention of PTSD will vary as a function of the need for technical expertise in mental health (e.g., the less dependent on mental health, the greater likelihood for wider distribution
- Specialists outside of mental health may be ideally suited to lead pharmacologic treatment trials for preventing PTSD